UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,108	02/13/2007	Pradman Qasba	65431(47992)	9769

21874 7590 10/13/2010

EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
10/13/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,108	QASBA ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,43-45 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 43-45 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-2, 43-45 and 49 are pending and being acted upon in this Office Action.

2. The objection to claim 2 has been obviated by the claim amendment filed August 2, 2010.

3. The Declaration of Pradman Qasba and Boopathy Ramakrishnan filed on August 2, 2010 under 37 CFR 1.131 is sufficient to overcome the Vocadlo et al reference.

4. The Declaration of Pradman Qasba and Boopathy Ramakrishnan under 37 CFR 1.132 filed August 2, 2010 is sufficient to overcome the rejection of claims 1-3 and 45 based upon US Pat No 7,332,355 (claimed priority to provisional application 60/523,523 filed November 18, 2003; PTO 892).

5. Applicant's arguments see 14-15, filed August 2, 2010, with respect to claims 1-2, 43-45 and 49 have been fully considered and are persuasive. The rejection of claims 1-2, 43-45 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 7,265,085 (of record, issued Sept 4, 2007; PTO 892) in view of US Pat No. 7,332,335 (claimed earliest priority to 60/523,523, filed November 18, 2003), Ramakrishnan et al (of record, J Biol Chem 277(23): 20833-20839, June 2002; PTO 892) and/or Hang et al (of record, J Am Chem 123: 1242-1243, 2001; PTO 1449) has been withdrawn. Specifically, without the '335 patent, the motivation to combine the '085, and Ramakrishnan et al or Hang et al is not apparent to one of ordinary skill in the art at the time the invention was made.

6. In view of the amendment filed August 2, 2010, the following rejections remain.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-2, 43-45 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a targeted glycoconjugate comprising a specific bioactive agent as listed at pages 14-15 and a specific targeting compound such as the ones listed at page 19 wherein the bioactive agent and the targeting compound are joined by a modified UDP galactose-Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring and wherein the targeted glycoconjugate is produced using the mutant Y289L O-GlcNAc glycosyltransferase, **does not** reasonably provide enablement for (1) any targeted glycoconjugate as set forth in claim 1, (2) any targeted glycoconjugate comprising any and all bioactive agent bioactive agent is any "polypeptide", any "releasing factor", any "releasing factor inhibitor", any "carbohydrate", any "nucleic acid", any "vaccine", any "receptor agonist", any "receptor antagonist", any cough and cold preparation, any enzyme inhibitor; any genetic material; any vitamin; or any herbal remedy and any and all targeting compound such as any glycoprotein, any glycolipid, or any carbohydrate wherein the bioactive agent and the targeting compound are joined by a modified UDP galactose acetyl group (UDP-GalNAc) comprises a ketone group attached to the C2 position of the galactose ring, (3) any pharmaceutical composition comprising any glycoconjugate mentioned above and a pharmaceutical acceptable carrier, (4) a kit comprising any glycoconjugate mentioned above and instruction for use in any therapeutic method, and (5) any targeted glycoconjugate comprising any bioactive agent and any antibody as the targeting compound wherein the bioactive agent and the targeting compound are joined by a modified UDP galactose-Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The claims encompass enormous number of targeted glycoconjugate comprising any unspecified bioactive agent and any unspecified targeting compound such as any glycoprotein, any glycolipid, any carbohydrate, or any antibody wherein the bioactive agent and the targeting compound are joined by any modified UDP galactose acetyl group having a ketone attached to the C2 position of the galactose ring as a pharmaceutical composition for use in any and all therapeutic methods.

Enablement is not commensurate in scope with *how to use* any unspecified targeted glycoconjugate comprising any bioactive agent and any unspecified targeting compound for the claimed targeted glycoconjugate as a pharmaceutical composition for use in medical therapy without guidance as to the binding specificity of such targeting compound.

The specification discloses only labeling of CREB or bovine lens α-crystallin using recombinant O-GlcNAc glycosylated CREB and the mutant Y289L O-GlcNAc glycosyltransferase, see pages 45-46. The specification discloses only modified UDP galactose--Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring using mutant Y289L galactose transferase, see page 48 of the specification and summary of the specification.

The specification suggests the use of known bioactive agent such as chemotherapeutic agent, toxin, alkylating agent, anti-proliferative agent, tubulin binding agents, mitomysins, bleomycins, diyenes, paclitaxel, doxetaxel, camptothecin aminocamptothecin, 9-nitrocamptotheein, 10-hydroxy-camptothecin, irinotecan, adriamycin, daunombicin, methotrexate, methopterin, dichloromethotrexate, mitomycin C, porfiromycin, 5-fluorouracil, 6-mercaptopurine, aminopterin, cytosine arabinoside, caminomycin, topotecan, 20-O-glucopyranosyl camptothecin), taxanes (baccatins, cephalomannine, carboplafin, cisplatin, interferon-2A, interferon-2B, interferon-N3, 6-azauridine, aclacinomycin(s), ancitabine, azacitadine, … etoposide or etoposide phosphate, melphalan, leurosidine, vindesine, leurosine, vinorelbine, vincristine and vinblastine or diagnostic agent to relevant cancer cells or tissue using monoclonal and polyclonal anti-CD20 antibody, anti-IL-2Ra antibody, anti-B-FN antibody and binding fragments thereof, Type I interferon, Type II interferon, cytokines (e.g., interleukine-1 "IL-1", interleukin-2 ("IL-2"), interleukin-3 ("IL-3"), interleukin-4 ("IL-4"), interleukin-5, interleukin-6, Interleuldn-7, interleukin-8 ("IL-8"), Interleukin- 10 ("IL- 10"), Interleukin- 11 ("IL- 11"), interleukin- 12 ("1L- 12"), interleukin- 13 ("1L- 13") and tumor necrosis factor ("TNF(α')), epidermal growth factor (EGF), transforming growth factor-β, vascular epithelial growth factor ("VEGF"), transforming growth factor-alpha

("TGFα"), folate, vitamin-B12, vitamin B6, niacin, nicotinamide, vitamin A, ferritin and vitamin D, steroids, hormones, cofactors, cyclosporin-A, prostaglandin and prostacyclin.

Other than the specific name bioactive agent and antibody attached to the C2 position of the galactose ring using modified enzyme Y289L O-GlcNAc glycosyltransferase, the specification does not teach the structure associated with function of any active agent is any "polypeptide", any "releasing factor", any "releasing factor inhibitor", any "carbohydrate", any "nucleic acid", any "vaccine", any "receptor agonist", any "receptor antagonist", any cough and cold preparation, any enzyme inhibitor; any genetic material; any vitamin; or any herbal remedy. Further, there is insufficient guidance as to the binding specificity of any targeting compound such as any glycoprotein, any glycolipid, any carbohydrate or any antibody so that the glycoconjugate could be target to the particular site.

Given the enormous number of unspecified glycoconjugate, there is a lack of in vivo working example of treating any and all diseases for the claimed pharmaceutical composition or for use in any therapeutic method.

As stated in the MPEP, when a compound or composition claim is limited by a particular use, i.e., medical use, enablement of that claim should be evaluated based on that limitation. See *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (claiming a chimeric gene capable of being expressed in any cyanobacterium and thus defining the claimed gene by its use), see MPEP 2164.01(c).

Furthermore, the specification defines the term "treat" or "treating" to include treating, *preventing*, ameliorating, or inhibiting a disease, disorder and/or a symptom of a disease and/or a disorder of an organism, see page 5, lines 1-3.

The specification defines the term "bioactive agent" means any chemical or biological material or compound suitable for delivery that induces a desired effect in or on an organism, such as a biological or pharmacological effect, which may include, but is *not limited to*, (1) having a *prophylactic effect* on the organism and preventing an undesired biological effect such as preventing an infection, (2) alleviating a condition caused by a disease or disorder, for example, alleviating pain or inflammation caused as a result of the disease or disorder, and/or (3) either alleviating, reducing, or completely eliminating the disease or disorder from the organism. As used herein, "bioactive agent" also refers to a substance which may be used in connection with an application that is therapeutic or diagnostic in nature, such as in methods for diagnosing the

presence or absence of a disease or disorder in a patient and/or in methods for the treatment or *prevention* of a disease or disorder in a patient. As used herein, "bioactive agent" refers also to substances which are capable of exerting a biological effect in vitro and/or in vivo. Examples of suitable bioactive agents include diagnostic agents, pharmaceuticals, drugs, synthetic organic molecules, proteins, peptides, vitamins, steroids and genetic material, including nucleosides, nucleotides and polynucleotides.

In this case, the specification provided little guidance as to the binding specificity of the targeting compound beyond the mere mentioned of a laundry list of targeting molecules, covalently linked to a laundry list of bioactive agent covalently linked together using a genetically engineered modified galactosyltransferase Y289L to append a ketone group at the carbon 2 of the UPD-GalNac.

With respect to claim 2, there is a lack of guidance as to the structure, i.e., amino acid sequence associated with function of any "polypeptide", any releasing factor, and any releasing factor inhibitor. There is a lack of guidance as to the structure, i.e., nucleic acid sequence associated with function of any nucleic acid. There is no specific guidance and working example of any vaccine or herbal remedy targeted glycoconjugate for prevention or treatment of any diseases. Applicants have not provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably corrected with the of scope of the claim broadly include a genus of targeted glycoconjugate comprising any glycoprotein, any glycolipid any carbohydrate, any polypeptide, any vaccine, any nucleic acid having any activity or function joined to any targeting compound by a modified UDP galactose acetyl group comprises a ketone group attached to the C2 position of the galactose ring.

For example, it is established in the art that there is a high degree of unpredictability in determining the structure of a given protein because a protein's structure is dependent on its given amino acid sequence and cannot be determined a *priori* and the function of a given protein is also highly unpredictable and variable and cannot necessarily be linked to a given structure. As evidenced by Jones et al (Pharmacogenomics Journal, 1:126-134, 2001; PTO 892), protein structure "prediction models are still not capable of producing accurate models in the vast majority of cases" (page 133, 3rd paragraph). Furthermore, Tosatto et al state, "the link between structure and function is still an open question and a matter of debate" (Current Pharmaceutical Design; 12:2067-2086, 2006, page 2075, 1st new paragraph). Until the structure of such

polypeptide, nucleic acid, "releasing factor", "releasing factor inhibitor", "carbohydrate", "vaccine", "receptor agonist", "receptor antagonist", enzyme inhibitor; genetic material; any vitamin; or any herbal remedy have been identified to have which particular function, it is unpredictable which unspecified bioactive agent is effective as a pharmaceutical for treating which disease. Given an enormous number of unspecified bioactive agents and unspecified targeting compounds in the claimed glycoconjugate, there is a lack of *in vivo* working example of such glycoconjugate could treat which out of many diseases, much less prevention of any and all diseases, including AIDS in a therapeutic method or medical therapy. Accordingly, it would require undue experimentation to use the invention in a manner commensurate in scope with the claims.

A pharmaceutical composition in the absence of *in vivo* data are unpredictable for the following reasons: (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for *in vivo* therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Even if the targeting compound is an antibody (claim 49), there is insufficient guidance as to the binding specificity of such antibody joined to any and all unspecified bioactive agent. The specification does not adequately teach how to effectively treat any diseases or diagnosing any diseases using any unspecified targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide without guidance as to the binding specificity of such glycoconjugate to the development of effective in vivo human therapeutic compositions, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the conjugate exemplified in the specification or the breadth of glycoconjugate for treating and preventing any diseases, encompassed by the claims.

Thus, Applicants have not provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably corrected with the of scope

of the claim broadly include a genus of targeted glycoconjugate comprising any glycoprotein, any glycolipid any carbohydrate, any polypeptide, any vaccine, any nucleic acid having any activity or function joined to any targeting compound by a modified UDP galactose acetyl group comprises a ketone group attached to the C2 position of the galactose ring. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Note, amending the claims to recite a glycoconjugate comprising a specific bioactive agent as shown the specific anticancer agent listed at pages 14-15 and a specific targeting compound such as the ones listed at page 19 wherein the bioactive agent and the specific targeting compound are joined by a modified UDP galactose-Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring using the mutant Y289L galactose transferase would obviate this rejection. One of ordinary skill in the art would be able to make and use the specific targeted glycoconjugate for delivery or targeting biological agent to cancer cell.

Applicants' arguments filed August 2, 2010 have been fully considered but are not found persuasive.

Applicants' position is that the instant claims are directed to a targeted glycoconjugate comprising a bioactive agent and a targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group (UDP-GalNAc) and wherein the UDP-GalNAc comprises a ketone group attached to the C2 position of the galactose ring.

Galactose is a well known saccharide to any person skilled in the art. The Specification teaches that the C2 position is favorable over other positions on the galactose ring because GalT

has been shown to tolerate unnatural substrates containing minor substitutions at the C2 positions. For example, at page 48 of the specification, Applicants describe a strategy for the rapid and sensitive detection of O-GlcNAc glycosylated proteins, where experiments show that C2 ketone functionality was appended at the C-2 position of the galactose ring because GalT has been shown to tolerate unnatural substrates containing minor substitutions at the C-2 positions, including 2-deoxy, 2-amino, and 2-N-acetyl substituent (Ian et al., 2001; Wong et el., 1995) (and)... 2-deoxy-Gal was transferred at rates comparable to Gel, whereas 3-, 4, and 6-deoxy-Gal were transferred at reduced rates." (page 48).

The present invention features glycoconjugates in which a bioactive agent is bound through a modified saccharide residue, e.g., UDP-GalNAc, to a compound which has an affinity for a target cell.

In the Examples, Applicants describe the rapid and sensitive detection of O-GlcNAc glycosylated proteins. As described by Applicants at page 48 of the specification, "the approach capitalizes on the substrate tolerance of GalT, which allows for chemoselective installation of an unnatural ketone functionality to O-GlcNAc modified proteins. The ketone moiety has been well-characterized in cellular systems as a neutral, yet versatile, chemical handle (Cornish et al., 1996; Mahal et al., 1997; Datta et al., 2002). Here, it serves as a unique marker to "tag" O-GlcNAc glycosylated proteins with biotin. Once biotinylated, the glycoconjugates can be readily detected by chemiluminescence using streptavidin conjugated to horseradish peroxidase (HRP)." (line 14 - 21).

As described in the specification at page 10, line 15, "the targeting compound (T)...is covalently bonded to a saccharide residue (S) with the use of a galactosyltransferase enzyme, preferably beta-1,4-galactosyltransferase (GalT). In one embodiment of the invention, a modified saccharide (S) is covalently associated with the targeting compound with the use of a genetically engineered GalT, such as Y289L GalT (as discussed above). **The targeting compound can be any naturally occurring glycoprotein, glycolipid or carbohydrate or can be engineered, through chemical or recombinant techniques.** For example, if the targeting compound does not include a GlcNAc residue, the compound can be engineered, either through recombinant or chemical techniques known in the art, so as to include such a residue. Preferably, the targeting compound includes an N-acetylglucosamine (GlcNAc) residue."

Moreover, binding specificity of glycoprotein, glycolipid or carbohydrate targeting compounds was known in the art at the time of filing. For example, antibodies were known in the

art at the time of filing to be targeting compounds. In particular, monoclonal antibodies against tumor antigens were known in the art as cancer therapeutic agents at the time of filing. For example, clinical trials were conducted with various monoclonal antibody therapeutics, such as bevacizumab, a recombinant humanized anti-VEGF monoclonal antibody that has been evaluated in Phase II and Phase II trials, and Ramaswamy et al. (Clin Breast Cancer. 2003 Oct;4(4):292-4, provided herein) describe in combination with doclataxel in women with advanced breast cancer. Vande Putte et al. (Ann Rheum Dis. 2003 Dec;62(12): 1168-77, provided herein), evaluate the efficacy and safety of the fully human anti-tumor necrosis factor alpha monoclonal antibody adalimumab (D2E7) in DMARD refractory patients with rheumatoid arthritis: a 12 week, phase II study. Carbohydrate based targeted therapeutics were also well known in the art. For example, insulin is a well known therapeutic. Poulsen et al. (Diabetes Care. 2003 Dec;26(12):3273-9, provided herein), test a combination therapy with insulin as part, rosiglitazone, and metformin to treat reduced insulin secretion and insulin resistance in skeletal muscle and liver in type 2 diabetes. Further, the anticancer compound doxorubicin was well known by one of skill in the art at the time of filing as a targeted anticancer compound. Numerous publications from the time of filing teach the use of doxorubicin in clinical trials (see, e.g. Anton et al., Clin Breast Cancer. 2003 Oct;4(4):286-91, provided herein).

Accordingly, these antibodies that have been described in the art have one N-linked bi-antennary oligosaccharide attached at the IgG-Fc region. The terminal sugars of the oligosaccharide moiety come in several glycoforms: for example, some are desialated, degalactosylated, with only terminal N-acetylglucosaminyl residues. The monoclonal antibodies carrying only terminal N-acetylglucosamine on the bi-antennary oligosaccharide moieties, the Go glycoform, can be generated by de-sialylation and de-galactosylation of the monoclonal antibodies. With the mutant Tyr289Leu-Gal-T1 and UDP-α-galactose-that is C2-modified, a galactose moiety, that has a chemically reactive group attached at the C2 position of galactose, can then be transferred to Go glycoform of the monoclonal antibody. In the Tyr289Leu-Gal-T1 described in the present invention, the binding pocket for UDP-α-galactose has been enlarged to accommodate modifications at C2 position of galactose, for example the ketone moiety that can serve as a neutral, yet versatile chemical handle.

To these monoclonal antibodies (or any other glycoprotein, glycolipid or carbohydrate targeting compound), that carry the modified galactose with the reactive functional group, it is possible to couple any other agent.

In response, the claims are not drawn to *a method making* targeted glycoconjugate from their individual components such as the known bioactive agent and known targeting compound joined by a modified saccharide compound which comprises galactose and reactive functional group attached to the C2 position of the galactose ring using the mutant Tyr289Leu-Gal-T1 and UDP-α-galactose that able to modified the galactose ring as argued.

Claim 1 encompasses any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

Claim 2 encompasses a genus of targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any polypeptide, any releasing factor, any releasing factor inhibitor, any carbohydrate, any nucleic acid, any migraine preparation, any sympathomimetic, any xanthine derivative, any cough and cold preparation, any genetic material, any vitamin, any herbal remedy joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

Claim 43 encompasses a pharmaceutical composition comprising any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

Claim 44 encompasses a kit comprising any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring and instructions for any use in therapeutic or diagnostic method.

Claim 45 encompasses a genus of targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring for use in medical therapy.

Claim 49 encompasses a genus of targeted glycoconjugate comprising any bioactive agent and any targeting compound such as any antibody wherein bioactive agent and antibody joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

None of the rejected claims are drawn to any known antibody or known bioactive agent as argued.

While the specification teaches how to make glycoconjugate by joining known antibody and known specific bioactive agent with the use of a modified galactosyltranserfase enzyme, beta-1,4-galactosyltransferase (GalT) through the modified UDP-GalNAc comprises a ketone group attached to the C2 position of the galactose ring, the specification does not teach how to use any glycoconjugate any bioactive agent and any targeting compound wherein the targeting agent is any glycoprotein, any glycolipid, any carbohydrate lacking any specificity joined to any bioactive agent such as any "polypeptide", any "releasing factor", any "releasing factor inhibitor", any "carbohydrate", any "nucleic acid", any "vaccine", any "receptor agonist", any "receptor antagonist", any cough and cold preparation, any enzyme inhibitor; any genetic material; any vitamin; or any herbal remedy as a pharmaceutical composition for treating and/or preventing any disease, or medical therapy.

There is a lack of guidance as to the structure, i.e., nucleic acid sequence associated with function of any nucleic acid. There is no specific guidance and working example of any vaccine or herbal remedy targeted glycoconjugate for prevention or treatment of any diseases. Applicants have not provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably corrected with the of scope of the claim broadly include a genus of targeted glycoconjugate comprising any glycoprotein, any glycolipid any carbohydrate, any polypeptide, any vaccine, any nucleic acid having any activity or function joined to any targeting compound by a modified UDP galactose acetyl group comprises a ketone group attached to the C2 position of the galactose ring.

For example, it is established in the art that there is a high degree of unpredictability in determining the structure of a given protein because a protein's structure is dependent on its given amino acid sequence and cannot be determined a *priori* and the function of a given protein is also highly unpredictable and variable and cannot necessarily be linked to a given structure. As evidenced by Jones et al (Pharmacogenomics Journal, 1:126-134, 2001; PTO 892), protein structure "prediction models are still not capable of producing accurate models in the vast majority of cases" (page 133, 3rd paragraph). Furthermore, Tosatto et al state, "the link between structure and function is still an open question and a matter of debate" (Current Pharmaceutical Design; 12:2067-2086, 2006, page 2075, 1st new paragraph). Until the structure of such polypeptide, nucleic acid, "releasing factor", "releasing factor inhibitor", "carbohydrate", "vaccine", "receptor agonist", "receptor antagonist", enzyme inhibitor; genetic material; any vitamin; or any herbal remedy have been identified to have which particular function, it is unpredictable which unspecified bioactive agent is effective as a pharmaceutical composition for treating which disease. Given an enormous number of unspecified bioactive agents and unspecified targeting compounds in the claimed glycoconjugate, there is a lack of *in vivo* working example of such glycoconjugate could treat which out of many diseases, much less prevention of any and all diseases, including AIDS in a therapeutic method or medical therapy. A pharmaceutical composition in the absence of *in vivo* data are unpredictable for the following reasons: (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for *in vivo* therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). Accordingly, it would require undue experimentation to use the invention in a manner commensurate in scope with the claims.

With respect to the argument antibodies were known in the art at the time of filing to be targeting compounds, it is noted that claims 1, 2, 43, 44 and 45 do not recite the targeting compound is antibody as argued. In addition to the lack of guidance as to the structure and function of the bioactive agent mentioned above in the claimed targeted glycoconjugate, the binding specificity of any targeting compound such as any glycoprotein, any glycolipid, any

carbohydrate or any antibody in the claimed targeted glycoconjugate is not defined. As such, it is unpredictable as to where and what the glycoconjugate target when administer as a pharmaceutical composition for treating and/or preventing any and all diseases. Therefore, it is not clear that the skilled artisan could predict the efficacy of which unspecific glycoconjugate exemplified in the specification or the breadth of glycoconjugate for treating and preventing any diseases as encompassed by the claims.

Thus, Applicants have not provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably corrected with the of scope of the claim broadly include a genus of targeted glycoconjugate comprising any glycoprotein, any glycolipid any carbohydrate, any polypeptide, any vaccine, any nucleic acid having any activity or function joined to any targeting compound by a modified UDP galactose acetyl group comprises a ketone group attached to the C2 position of the galactose ring. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Without sufficient guidance, making and using targeted glycoconjugate comprising any glycoprotein, any glycolipid, any carbohydrate, any polypeptide, any releasing factor, any releasing factor inhibitor, any nucleic acid, any vaccine, any receptor agonist, any receptor antagonist any enzyme inhibitor, any cough and cold preparation, any vitamin, any herbal remedy, any genetic material, any migraine preparation, any xanthine derivative joined to any targeting compound, any targeting compound such as any glycoprotein, any glycolipid, any carbohydrate or any antibody through a modified UDP-GalNAc comprises a ketone group attached to the C2 position of the galactose ring as a pharmaceutical composition would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. For these reasons, the rejection is maintained.

9. Claims 1-2, 43-45 and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claim 1 encompasses any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting

compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

Claim 2 encompasses a genus of targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any polypeptide, any releasing factor, any releasing factor inhibitor, any carbohydrate, any nucleic acid, any migraine preparation, any sympathomimetic, any xanthine derivative, any cough and cold preparation, any genetic material, any vitamin, any herbal remedy joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

Claim 43 encompasses a pharmaceutical composition comprising any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

Claim 44 encompasses a kit comprising any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring and instructions for any use in therapeutic or diagnostic method.

Claim 45 encompasses a genus of targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring for use in medical therapy.

Claim 49 encompasses a genus of targeted glycoconjugate comprising any bioactive agent and any targeting compound such as any antibody wherein bioactive agent and antibody joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

The scope of the each genus of targeting compound and bioactive agent includes many members with widely differing structural, chemical, and physiochemical properties of any bioactive agent, and targeting compound such as widely differing amino acid sequences, nucleotide sequences, and biological functions in the claimed glycoconjugate. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provides only the bovine sequence.

In this case, the specification does not reasonably provide a **written description** for (1) the *binding specificity* of the targeting compound such as any glycoprotein, any glycolipid, any carbohydrate or any antibody in the claimed glycoconjugate and (2) the structure associated with function of any bioactive agent, any bioactive agent such as any polypeptide, any releasing factor, any releasing factor inhibitor, any nucleic acid, any vaccine, any xanthine derivative, any genetic material, any herbal remedy joined to any targeting compound by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring for use in any medical therapy that encompassed prevention of all diseases.

At the time of filing, the specification discloses only labeling of CREB or bovine lens α-crystallin using recombinant O-GlcNAc glycosylated CREB and the mutant Y289L O-GlcNAc glycosyltransferase, see pages 45-46. The specification discloses only modified UDP galactose-–Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring using mutant Y289L galactose transferase, see page 48 of the specification and summary of the specification.

The specification suggests the use of glycoconjugate for delivery of bioactive agent such as chemotherapeutic agent, toxin, alkylating agent, anti-proliferative agent, tubulin binding agents, mitomycin, bleomycins, diyenes, paclitaxel, docetaxel, camptothecin aminocamptothecin, 9-nitrocamptothecin, 10-hydroxy-camptothecin, irinotecan, adriamycin, daunombicin, methotrexate, methopterin, dichloromethotrexate, mitomycin C, porfiromycin, 5-fluorouracil, 6-mercaptopurine, aminopterin, cytosine arabinoside, caminomycin, topotecan, 20-O-glucopyranosyl camptothecin), taxanes (baccatins, cephalomannine, carboplafin, cisplatin, interferon-2A, interferon-2B, interferon-N3, aclacinomycin(s), ancitabine, azacitadine, … vindesine, leurosine, vinorelbine, vincristine and vinblastine or diagnostic agent to relevant cancer cells or tissue using monoclonal and polyclonal anti-CD20 antibody, anti-IL-2Ra antibody, anti-B-FN antibody and binding fragments thereof, Type I interferon, Type II interferon, cytokines (e.g., interleukine-1 "IL-1", interleukin-2 ("IL-2", interleukin-3 ("IL-3"), interleukin-4 ("IL-4"), interleukin-5, interleukin-6, Interleuldn-7, interleukin-8 ("IL-8"), Interleukin- 10 ("IL- 10"), Interleukin- 11 ("IL- 11"), interleukin- 12 ("IL- 12"), interleukin- 13 ("IL- 13") and tumor necrosis factor ("TNF(α')), epidermal growth factor (EGF), transforming growth factor-β, vascular epithelial growth factor ("VEGF"), transforming growth factor-alpha ("TGFα"), folate, vitamin-B12, vitamin B6, niacin, nicotinamide, vitamin A, ferritin and vitamin D, steroids, hormones, cofactors, cyclosporin-A, prostaglandin and prostacyclin.

Beside the known bioactive agent and known targeting antibody joined together using a mutant Y289L galactose transferase that modified UDP-GalNAc comprises a ketone group attached to the C2 position of the galactose ring, applicants are not in possession of any targeted glycoconjugate because the structure associated with function of any bioactive agent such as any "polypeptide", any "releasing factor", any "releasing factor inhibitor", any "carbohydrate", any "nucleic acid", any "vaccine", any "receptor agonist", any "receptor antagonist", any cough and cold preparation, any enzyme inhibitor; any genetic material; any vitamin; or any herbal remedy is not adequately described. The disclosure does not allow one of skill in the art to visualize or recognize

the structure of such polypeptide, releasing factor, releasing factor inhibitor, carbohydrate, nucleic acid, migraine preparation, sympathomimetic, xanthine derivative, cough and cold preparation, genetic material, vitamin, or herbal remedy as bioactive agent joined to any targeting compound, any targeting compound such as any glycoprotein, any glycolipid, any carbohydrate required to practice the claimed invention.

Furthermore, the specification provided little or no guidance as to the *binding specificity* of the targeting compound beyond the mere mentioned of a laundry list of targeting molecules. The term "glycoprotein", "glycolipid", "carbohydrate" or "antibody" does not enable one of ordinary skilled in the art to envision the binding specificity of such for the claimed targeted glycoconjugate.

The specification defines the term "pharmaceutical" or "drug" refers to any therapeutic or *prophylactic* bioactive agent which may be used in the treatment (including the prevention, diagnosis, alleviation, or cure) of a malady, affliction disease, disorder or injury in a patient. Therapeutically useful peptide, polypeptides and polynucleotides may be included within the meaning of the term pharmaceutical or drug.

There is no disclosure of any *in vivo* working example that the claimed glycoconjugate could treat any disease such as AIDS, cancer, any autoimmune diseases, any bacterial infections, any psychiatric diseases, any cardiovascular diseases, etc, much less preventing any diseases.

It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different pharmacological activities. Because of the lack of sufficient guidance and predictability in determining which unspecified targeted glycoconjugate would lead to which function or activity in vivo, it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of bioactive agent in the claimed targeted glycoconjugate as pharmaceutical composition.

For example, it is established in the art that there is a high degree of unpredictability in determining the structure of a given protein because a protein's structure is dependent on its given amino acid sequence and cannot be determined a *priori* and the function of a given protein is also highly unpredictable and variable and cannot necessarily be linked to a given structure. As evidenced by Jones et al (Pharmacogenomics Journal, 1:126-134, 2001; PTO 892), protein structure "prediction models are still not capable of producing accurate models in the vast

majority of cases" (page 133, 3rd paragraph). Furthermore, Tosatto et al state, "the link between structure and function is still an open question and a matter of debate" (Current Pharmaceutical Design; 12:2067-2086, 2006, page 2075, 1st new paragraph). Until the structure of such polypeptide, nucleic acid, "releasing factor", "releasing factor inhibitor", "carbohydrate", "vaccine", "receptor agonist", "receptor antagonist", enzyme inhibitor; genetic material; any vitamin; or any herbal remedy have been identified to have which particular function, it is unpredictable which unspecified bioactive agent is effective as a pharmaceutical composition for treating which disease. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel,* 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Further, possession may not be shown by merely described how to obtain possession of members of the claimed genus or how to identify their common structural features. See University of Rochester, 358 F.3d at 927, 69 USPQ2d at 1895.

Accordingly, the specification fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph, with respect to the full scope of claims 1-2, 43-45 and 49.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001and revision of the Written Description Training materials, posed April 11, 2008 http://www.USPTO.gov/web/menu/written.pdf.

Note, amending the claims to recite a glycoconjugate comprising a specific bioactive agent as listed at pages 14-15 and a specific targeting compound such as the ones listed at page 19 wherein the bioactive agent and the targeting compound are joined by a modified UDP galactose-Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring using the mutant Y289L galactose transferase would obviate this rejection. One of ordinary skill in the art would be able to envision the structure associated with function of the encompassed claimed glycoconjugate for delivery or targeting the specific biological agent to cancer cell.

Applicants' arguments filed August 2, 2010 have been fully considered but are not found persuasive.

Applicants' position is that as amended, the claims to particularly recite targeted glycoconjugate compounds comprising a bioactive agent and a targeting compound, wherein the bioactive agent and targeting compound are linked by a modified UDP galactose acetyl group (UDP-GalNAc) and wherein the modified UDP-GalNAc comprises a ketone group attached to the C2 position of the galactose ring. Targeted glycoconjugate compounds are described at page 8. Modified saccharide compounds are described at page 9. Targeting compounds are described at page 10, page 18. Bioactive agents are described beginning at page 10.

Applicants describe a strategy for the rapid and sensitive detection of O-GlcNAc glycosylated proteins, where experiments show that "the ketone functionality was appended at the C-2 position of the galactose ring because GalT has been shown to tolerate unnatural substrates containing minor substitutions at the C-2 position including 2-deoxy, 2-arnino, and 2-N-acety] substituent (lan et al., 2001: Wong et al,1995) (and)... 2-deoxy-Gal was transferred at rates comparable to Gat, whereas 3, 4 and 6 deoxy Gal were transferred at reduced rates.'" (page 48).

Applicants submit that the claims are sufficiently described in the specification to reasonably convey to one skilled in the relevant art that The inventor, at the lime the application was filed, had possession of the claimed invention, Applicants respectfully request that the forgoing rejections be withdrawn.

In response, the claims are not drawn to a method making targeted glycoconjugate from their individual components such as bioactive agent and targeting compound joined by a modified

saccharide compound which comprises galactose and reactive functional group attached to the C2 position of the galactose ring.

Claim 1 encompasses any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

Claim 2 encompasses a genus of targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any polypeptide, any releasing factor, any releasing factor inhibitor, any carbohydrate, any nucleic acid, any migraine preparation, any sympathomimetic, any xanthine derivative, any cough and cold preparation, any genetic material, any vitamin, any herbal remedy joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

Claim 43 encompasses a pharmaceutical composition comprising any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

Claim 44 encompasses a kit comprising any targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring and instructions for any use in therapeutic or diagnostic method.

Claim 45 encompasses a genus of targeted glycoconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent is any glycoprotein, any glycolipid, any carbohydrate joined to any targeting compound, wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the

modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring for use in medical therapy.

Claim 49 encompasses a genus of targeted glycoconjugate comprising any bioactive agent and any targeting compound such as any antibody wherein bioactive agent and antibody joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring.

None of the rejected claims are drawn to any known antibody or known bioactive agent as argued.

While the specification teaches how to make glycoconjugate by joining *known* antibody and known specific bioactive agent with the use of a modified galactosyltransferase enzyme, beta-1,4-galactosyltransferase (GalT) through the modified UDP-GalNAc comprises a ketone group attached to the C2 position of the galactose ring, applicants are not in possession of a genus of targeted glycoconjugate comprising any unspecified bioactive agent, any bioactive agent such as any polypeptide, any releasing factor, any releasing factor inhibitor, any carbohydrate, any nucleic acid, any migraine preparation, any sympathomimetic, any xanthine derivative, any cough and cold preparation, any genetic material, any vitamin, any herbal remedy as bioactive agent or glycoprotein, glycolipid, carbohydrate or antibody (i.e., six CDRs) because of the lack of guidance as to the structure of such. The skilled artisan cannot envision all the contemplated polypeptide, nucleotide sequence, derivative, genetic material, analogue, active ingredient in the herbal remedy by the detailed chemical structure of the claimed bioactive agent and therefore conception cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

At the time of filing, the specification fails to adequately describe this genus of polypeptide, releasing factor, releasing factor inhibitor, carbohydrate, nucleic acid, migraine preparation, sympathomimetic, derivative of xanthine, any cough and cold preparation, any genetic material, vitamin, and herbal remedy as there is no disclosure of any particularly

identifying (i.e., substantial) structural feature that is shared by the members of the genus of proteins, nucleic acid, antibody, mimetic, derivative which correlates with any particularly identifying functional feature, i.e., agonistic or antagonistic effect also shared by at least a substantial number of those members. As a consequence, the disclosure would not reasonably convey that Applicant had possession of the claimed invention at the time the application was filed because the disclosure would not permit the skilled artisan to immediately envision, recognize or distinguish members of the genus of polypeptide, releasing factor, releasing factor inhibitor, carbohydrate, nucleic acid, migraine preparation, sympathomimetic, derivative of xanthine, any cough and cold preparation, any genetic material, vitamin, and herbal remedy as bioactive agent or glycoprotein, glycolipid, carbohydrate or and antibody as a targeting compound having which binding specificity to which the claims are directed.

For example, it is established in the art that there is a high degree of unpredictability in determining the structure of a given protein because a protein's structure is dependent on its given amino acid sequence and cannot be determined a *priori* and the function of a given protein is also highly unpredictable and variable and cannot necessarily be linked to a given structure. As evidenced by Jones et al (Pharmacogenomics Journal, 1:126-134, 2001; PTO 892), protein structure "prediction models are still not capable of producing accurate models in the vast majority of cases" (page 133, 3rd paragraph). Furthermore, Tosatto et al state, "the link between structure and function is still an open question and a matter of debate" (Current Pharmaceutical Design; 12:2067-2086, 2006, page 2075, 1st new paragraph).

Until the function or bioactivity of such unspecified bioactive agent has been identified and effective to treat which disease for use a pharmaceutical composition when linked to the known targeting compound or antibody, applicants are asking one of ordinary skill in the art to come up with the structure of such bioactive agent for the claimed targeted glycoconjugate wherein the bioactive agent and targeting compound are joined by a modified UDP galactose acetyl group, and wherein the modified UDP-GalNAc comprises a reactive functional group attached to the C2 position of the galactose ring as a pharmaceutical composition for treating any disease, or medical therapy. For these reasons, the rejection is maintained.

With respect to the argument antibodies were known in the art at the time of filing to be targeting compounds, it is noted that claims 1, 2, 43, 44 and 45 do not recite the targeting compound is antibody as argued. In addition to the lack of description as to the structure and function of the bioactive agent mentioned above in the claimed targeted glycoconjugate, the

binding specificity of any targeting compound such as any glycoprotein, any glycolipid, any carbohydrate or any antibody in the claimed targeted glycoconjugate is not defined. As such, it is unpredictable as to where and what the glycoconjugate target when administer as a pharmaceutical composition for treating and/or preventing any and all diseases. Therefore, the binding specificity of the targeted glycoconjugate as a pharmaceutical composition for use in therapeutic method is not adequately described. For these reasons, the rejection is maintained.

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The IFW official Fax number is (571) 273-8300.

13. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
October 8, 2010